REMARKS

Applicant thanks Examiner Li Zheng for having the telephonic interview on May 18, 2010. The following comments summarize (i) why Fabijanski et al. (US Patent 6,753,460) when taken as a complete document teaches away from the use of conditionally lethal genes for the production of transgenic plants that comprise recombinant traits of interest, and (ii) why it is not obvious to modify Fabijanski et al. and combine with conditional lethal gene. Such comments are provided as requested by Examiner during the interview.

As outlined below, Fabijanski et al. provide methods to contain the spread of DNA between plants. The method positively selects, i.e. kills, plants that do not comprise the desired genetic compliment. Fabijanski et al. also teach that the use of conditional lethal genes is not desired for this purpose.

As disclosed in the abstract, Fabijanski et al. "relates to methods to control the spread of recombinant DNA molecules between sexually compatible plants of differing genetic composition".

The Background of the Invention section of Fabijanski et al. state (column 1, lines 47-63 - emphasis added):

> Novel traits are introduced into plants by conventional breeding or genetic engineering. However, to date neither route provides features that can be routinely used for maintaining germplasm purity, or controlling persistence or potential spread of the novel trait. Current vectors and genetic compositions typically do not address two important issues: (1) commercial issues such as the prevention of transformed crop plants or elite varieties from contaminating other commercial productions, or the prevention of introgression of alien germplasm from closely related cultivars or plant species, and; (2) environmental issues such as the removal of transformed crop plants or related species that have acquired the genes in question from non-agricultural environments. Additionally current transformation methods do not provide the means for reducing the introduction of

> genes via pollen mediated out-crossing to other cultivars or related species (either wild or cultivated).

The disclosure provides a discussion identifying areas where cross-contamination can occur and the concerns associated with cross-contamination (see column 1, line 64 to column 4, line 25). In summary Fabijanski et al. states "[a]ccordingly there is a need for methods to restrict the potential flow of this type of genes or to selectively eliminate those plants which contain such genes" (column 4, lines 25-27). Fabijanski et al. then goes on to discuss the use of conditionally lethal genes and states (column 4, lines 28-40 – emphasis added):

> Attempts have been made to develop methods to specifically remove or identify plants that contain novel traits introduced by recombinant DNA. For example, the use of a conditionally lethal gene, i.e. one which results in plant cell death under certain conditions, has been suggested as a means to selectively kill plant cells containing a specific recombinant DNA. Recently the development of genes which are conditionally lethal in plants have been described (eg WO 94/03619). However, methods using these genes have been restricted to the application of a substance that triggers the expression of the lethal phenotype. For widespread agricultural practices, these methods have serious limitations.

As discussed during the telephone interview, **the use of conditionally lethal genes to express a lethal phenotype and control cross-contamination requires an additional step in the process, that of applying chemicals in order to induce the lethal phenotype in the plant.** This extra step provides disadvantage in comparison with the instant claims. Fabijanski et al. concludes the disadvantages below (column 5, lines 25-31 – emphasis added):

> The need to apply a chemical to induce the lethal phenotype reduces the utility of a conditionally lethal gene. The widespread application of chemicals may be impractical and raise additional environmental concerns. Accordingly the use of conditionally lethal genes as currently described is not ideally suited for general applications since intervention is required to express the lethal phenotype. .

In conclusion, Fabijanski et al. states (column 6, lines 5-14):

> Therefore, a method that limits outcrossing and introgression without intervention is needed for management and control of novel traits and crops with novel traits. A mechanism to control cross-contaminations among commercial crops is also needed. Such a mechanism is also needed in the management of perennial crops such as trees, shrubs and grapevines. In particular any mechanism which does not require intervention in order to function is ideally suited for perennial crops. The present invention describes methods and genetic compositions which respond to these needs.

and in column 6, lines 17-23:

> The present invention comprises methods and recombinant DNA compositions that block the spread and persistence of genes in other cultivars of the same species or related species, resulting from unintended outcrossing by pollen produced by plants containing said recombinant DNA. The invention further ensures that introgression of alien germplasm is eliminated in a selfing population.

Therefore, although Fabijanski et al. provides a general disclosure of conditionally lethal genes that were known in the art at the time the application was filed, **the teaching of Fabijanski et al. is that these conditionally lethal genes have reduced utility, may be impractical and raise environmental concerns.** Therefore, the modification of Fabijanski et al.'s invention with conditionally lethal genes is not obvious to a person skilled in the art.

Throughout Fabijanski et al. it is noted that the invention requires expression of a repressable lethal gene, **not** a conditionally lethal gene.

The invention disclosed in Fabijanski et al., uses lethal genes to ensure that expression of a trait which does not comprise the full complement of the recombinant DNA is lethal to the plant. As disclosed at column 15, lines 24-38:

> ...methods and compositions are provided for a novel means of producing transgenic plants that contain two recombinant repressible lethal gene constructs. All plants comprising recombinant DNA resulting from outcrossing of the transgenic plant are rapidly eliminated from the environment. The first repressible lethal gene construct comprises a lethal gene and a repressor gene that blocks the expression of a second repressible lethal gene and optionally a gene encoding a novel trait of interest. The second repressible lethal gene construct comprises a second lethal gene and a repressor gene that blocks the expression of the first repressible lethal gene. Cells containing both genetic constructs produce two types of repressor molecules; hence both lethal genes remain in a repressed state.

The selection strategy used to control outcrossing uses positive selection to ensure both constructs are present within a plant. Expression of either the first or second repressible lethal gene construct without the other gene construct results in expression of the lethal gene. Any seed resulting from the union expresses the lethal gene and would be aborted. Furthermore, persistence of either the first or second repressible lethal gene construct in an unintended genotype (i.e. not comprising the complete recombinant DNA complement) is inhibited (see column 16, lines 16-24 of Fabijanski et al.).

Applicants respectfully submit that the entire teaching of Fabijanski et al., is directed to a method of controlling the spread of recombinant DNA molecules by production of transgenic plants that comprise recombinant traits of interest linked to repressible lethal genes, **not** a conditionally lethal gene.

Another difference between the instant claims and Fabijanski is sequential steps vs. a simultaneous step of introducing first and second nucleotide sequence into a plant. In the present invention, the first nucleotide sequence containing the first coding region encoding a repressible tag protein that is benign to the plant when expressed, is introduced into a transgenic plant or portion thereof to obtain a plant platform for subsequent transformation with the second nucleotide sequence as is disclosed in Example 5 of the present application. Unlike the system taught in Fabijanski et al that requires both the first and second nucleotide sequences to be introduced into the transgenic plant at the same time to ensure that the first coding region (lethal

gene) is repressed to allow the plant to survive, instant Claims 1 and 14 require sequential steps, i.e., the plant comprises a first sequence, and then the second sequence is introduced to the plant.

CONCLUSION

In view of the above, examination of the application on the merits and allowance is respectfully requested.

Respectfully submitted,

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